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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/550,163	04/14/00	ABBOTT	G 2323-150

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EXAMINER	
WHITEMAN, B	
ART UNIT	**PAPER NUMBER**
1633	8

DATE MAILED: 06/21/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/550,163	ABBOTT ET AL.	
	Examiner	Art Unit	
	Brian Whiteman	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-68 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claims 1-68 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15)☐ Notice of References Cited (PTO-892)
16)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18)☐ Interview Summary (PTO-413) Paper No(s). _____ .
19)☐ Notice of Informal Patent Application (PTO-152)
20)☐ Other: .

DETAILED ACTION

Claims 1-68 are pending and under consideration in the instant application.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1, 2, 3, 4, 5, 6, 7, 8, 9, and 24-30, drawn to a nucleic acid comprising a nucleotide sequence coding for human MiRP1 set forth in SEQ ID NO: 2 or its complement; a nucleic acid which hybridizes under stringent conditions with a nucleic acid of (a); a nucleic acid which has at least 90% identity with the nucleic acid of (a); drawn to an allele specific probe or primer which hybridizes to the DNA of SEQ ID NO: 2 or its complement of claim 1; a method of amplifying an exon of KCNE2 wherein said method comprises using a pair or primers; a cell transfected with the DNA of SEQ ID NO: 2 or its complement; a vector comprising the isolated DNA of SEQ ID NO: 2 of claim 1, classifiable in class 536, subclass 23.1.

II. Claims 1, 5-7, 25, 27, and 29, drawn to a nucleic acid comprising a nucleotide sequence coding for rat MiRP1 set forth in SEQ ID NO: 4 or its complement; a nucleic acid which hybridizes under stringent conditions with a nucleic acid of (b); a nucleic acid which has at least 90% identity with the nucleic acid of (b); a cell transfected with the DNA of SEQ ID NO: 4 or its complement; a vector comprising the isolated DNA of SEQ ID NO: 4 of claim 1, classifiable in class 536, subclass 23.1.

III. Claims 1, 5-7, and 25, 27, and 29, drawn to a nucleic acid comprising a nucleotide sequence coding for human MiRP2 set forth in SEQ ID NO: 6 or its complement; a nucleic acid which hybridizes under stringent conditions with a nucleic acid of (c); a nucleic acid which has at least 90% identity with the nucleic acid of (c); an allele specific probe or primer which hybridizes to the DNA of SEQ ID NO: 6 or its complement of claim 1; a cell transfected with the DNA of SEQ ID NO: 6 or its complement; a vector comprising the isolated DNA of SEQ ID NO: 6 of claim 1, classifiable in class 536, subclass 23.1.

IV Claims 1, 5-7, and 25, 27, and 29, drawn to a nucleic acid comprising a nucleotide sequence coding for mouse MiRP2 set forth in SEQ ID NO: 8 or its complement; a nucleic acid which hybridizes under stringent conditions with a nucleic acid of any one of (d), a nucleic acid which has at least 90% identity with the nucleic acid of (d); an allele specific probe or primer which hybridizes to the DNA of SEQ ID NO: 8 or its complement of claim 1; a cell transfected with the DNA of SEQ ID NO: 8 or its complement; a vector comprising the isolated DNA of SEQ ID NO: 8 of claim 1, classifiable in class 536, subclass 23.1.

V. Claims 1, 5-7, and 25, 27, and 29, drawn to a nucleic acid comprising a nucleotide sequence coding for human MiRP3 set forth in SEQ ID NO: 10 or its complement; a nucleic acid which hybridizes under stringent conditions with a nucleic acid of any one of (e); a nucleic acid which has at least 90% identity with the nucleic acid of (e); an allele specific probe or primer which hybridizes to the DNA of SEQ ID NO: 10 or its complement of claim 1; a cell transfected with the

DNA of SEQ ID NO: 10 or its complement; a vector comprising the isolated DNA of SEQ ID NO: 10 of claim 1, classifiable in class 536, subclass 23.1.

VI. Claims 1, 5-7, and 25, 27, and 29, drawn to a nucleic acid comprising a nucleotide sequence coding for mouse MiRP3 set forth in SEQ ID NO: 12 or its complement; a nucleic acid which hybridizes under stringent conditions with a nucleic acid of any one of (f); a nucleic acid which has at least 90% identity with the nucleic acid of (f); an allele specific probe or primer which hybridizes to the DNA of SEQ ID NO: 12 or its complement of claim 1 a cell transfected with the DNA of SEQ ID NO: 12 or its complement; a vector comprising the isolated DNA of SEQ ID NO: 12 of claim 1, classifiable in class 536, subclass 23.1.

VII. Claims 10-12, drawn to a method of diagnosing a polymorphism which causes long QT syndrome comprising hybridizing a probe of claim 3 to a patient's sample of DNA or RNA under stringent conditions which allow hybridization of said probe to nucleic acid comprising said polymorphism but prevent hybridization of said probe to a nucleic acid of SEQ ID NO: 1 wherein the presence of a hybridization signal indicates the presence of said polymorphism, classifiable in class 436, subclass 811.

VIII. Claims 15-18 and 20-22, drawn to an antibody which binds to a mutant KCNE2 polypeptide, wherein said mutant KCNE2 polypeptide has the amino acid sequence of SEQ ID NO: 2, with an altered sequence disclosed herein; a method for diagnosing long QT syndrome said method consisting of an assay for the presence of mutant KCNE2 polypeptide is a patient by reacting a patient's sample

with an antibody of claim 15; an antibody which specifically for a polypeptide of claim 19, classifiable in class 435, subclass 7.1.

IX. Claims 13 and 14, drawn to a method of diagnosing the presence of a polymorphism in human KCNE2 which causes long QT syndrome wherein said method is performed by means which identify the presence of said polymorphism is one which results in the presence of a KCNE2 polypeptide of SEQ ID NO: 2 with an altered amino acid, classifiable in class 436, subclass 811.

X. Claim 19, drawn to a polypeptide comprising an amino acid sequence set forth in SEQ ID NO: 2; a polypeptide having at least 90% identity to the polypeptide of (a), a polypeptide comprising an amino acid sequence set forth in SEQ ID NO: 2 with a mutation described herein, classifiable in class 530, subclass 350+.

XI. Claim 19, drawn to a polypeptide comprising an amino acid sequence set forth in SEQ ID NO: 4; a polypeptide having at least 90% identity to the polypeptide of (c), classifiable in class 530, subclass 350+.

XII. Claim 19, drawn to a polypeptide comprising an amino acid sequence set forth in SEQ ID NO: 6; a polypeptide having at least 90% identity to the polypeptide of (d), classifiable in class 530, subclass 350+.

XIII. Claim 19, drawn to a polypeptide comprising an amino acid sequence set forth in SEQ ID NO: 8; a polypeptide having at least 90% identity to the polypeptide of (e), classifiable in class 530, subclass 350+.

XIV. Claim 19, drawn to a polypeptide comprising an amino acid sequence set forth in SEQ ID NO: 10; a polypeptide having at least 90% identity to the polypeptide of (f), classifiable in class 530, subclass 350+.

XV. Claim 19, drawn to a polypeptide comprising an amino acid sequence set forth in SEQ ID NO: 12; a polypeptide having at least 90% identity to the polypeptide of (g), classifiable in class 530, subclass 350+.

XVI. Claim 31, drawn to a nonhuman, transgenic animal comprising a nucleotide sequence coding for human MiRP1 set forth in SEQ ID NO: 2 its complement; a nucleic acid which hybridizes under stringent conditions with a nucleic acid of (a); a nucleic acid which has at least 90% identity with the nucleic acid of (a), classifiable in class 800, subclass 8.

XVII. Claim 31, drawn to a nonhuman, transgenic animal comprising a nucleotide sequence coding for rat MiRP1 set forth in SEQ ID NO: 4 its complement; a nucleic acid which hybridizes under stringent conditions with a nucleic acid of (b); a nucleic acid which has at least 90% identity with the nucleic acid of (b), classifiable in class 800, subclass 8.

XVIII. Claim 31, drawn to a nonhuman, transgenic animal comprising a nucleotide sequence coding for human MiRP2 set forth in SEQ ID NO: 6 or its complement; a nucleic acid which hybridizes under stringent conditions with a nucleic acid of (c); a nucleic acid which has at least 90% identity with the nucleic acid of (c), classifiable in class 800, subclass 8.

XIX. Claim 31, drawn to a nonhuman, transgenic animal comprising a nucleotide sequence coding for mouse MiRP2 set forth in SEQ ID NO: 8 or its complement; a nucleic acid which hybridizes under stringent conditions with a nucleic acid of (d); a nucleic acid which has at least 90% identity with the nucleic acid of (d), classifiable in class 800, subclass 8.

XX. Claim 31, drawn to a nonhuman, transgenic animal comprising a nucleotide sequence coding for human MiRP3 set forth in SEQ ID NO: 10 or its complement; a nucleic acid which hybridizes under stringent conditions with a nucleic acid of (e); a nucleic acid which has at least 90% identity with the nucleic acid of (e), classifiable in class 800, subclass 8.

XXI. Claim 31, drawn to a nonhuman, transgenic animal comprising a nucleotide sequence coding for mouse MiRP3 set forth in SEQ ID NO: 12 or its complement; a nucleic acid which hybridizes under stringent conditions with a nucleic acid of (f); a nucleic acid which has at least 90% identity with the nucleic acid of (f), classifiable in class 800, subclass 8.

XXII. Claim 32, drawn to a non-human, transgenic animal comprising the DNA of claim 2, classifiable in class 800, subclass 8.

XXIII. Claims 33-43, drawn to a method to screen for drugs which are useful in treating a person with a mutation in KCNE2, wherein said method comprises: placing a first set of cells expressing KCNE2 with a mutation into a bathing solution to measure a first induced K+ current, classifiable in class 424, subclass 93.1.

XXIV. Claims 44-46 and 51-52, drawn to a method to screen drugs which are useful in treating or preventing long QT syndrome, said method comprising: preparing a transgenic animal cotransfected with wild-type HERG and mutant KCNE2; a non-human transgenic animal wherein said animal comprises wild-type human KCNE2 and mutant human HERG, classifiable in class 800, subclass 8.

XXV. Claim 47, drawn to a method of diagnosing a polymorphism which causes long QT syndrome comprising determining the KCNE2 sequence in a patient, classifiable in class 436, subclass 811.

XXVI. Claims 48-50, drawn to a method of determining the correlation between inheritance of a mutation in the KCNE2 gene; the method of claim 48, wherein said expression product is selected from the group consisting of mRNA of the KCNE2 gene, classifiable in class 436, subclass 811.

XXVII. Claims 53-58, drawn to a method for determining the ability of a drug to affect the fast delayed rectifier potassium current (I_{Kr}), classifiable in class 424, subclass 93.1.

XXVIII. Claims 59-62, drawn to a method for determining the correlation between inheritance of a mutation in the KCNE2 gene and reaction to a drug, classifiable in class 800, subclass 3.

XXIX. Claims 63-65, drawn to a mammal comprising a disruption in at least one allele of it endogenous KCNE2 gene, classifiable in class 800, subclass 8.

XXX. Claims 66, 67, and 68, drawn to a method of identifying a polymorphic form correlated with long QT syndrome, classifiable in class 436, subclass 811.

Claims 1, 5-7, and 25, 27, and 29 link(s) inventions I-VI. Claim 19 link(s) inventions X-XV. Claim 31 link(s) inventions XVI-XXI. The restriction requirement between the linked inventions is subject to the non-allowance of the linking claim(s), claims 1, 5-7, 19, 25, 27, 29, or 31. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or non-statutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. See *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

The inventions are distinct, each from the other because:

Inventions I-VI and VIII, X-XXII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, Inventions I-VI are directed to different nucleic acid sequences comprising (SEQ ID NO 2, 4, 6, 8, 10, 12). Invention VIII is directed to antibodies, which bind to a mutant KCNE2. Inventions X-XV are directed to different isolated polypeptide sequences comprising amino acid sequences set forth in (SEQ ID NO: 2, 4, 6, 8, 10,

and 12). Inventions XVI-XXI are directed to nonhuman, transgenic animals, each comprising of a separate nucleotide sequence (SEQ ID NO. 2, 4, 6, 8, 10, or 12). Invention XXII is directed to a nonhuman, transgenic animal comprising an isolated DNA encoding a polypeptide of SEQ ID NO: 2. Each nucleotide sequence of Inventions I-VI can be used in a separate method of gene therapy. In addition, the nucleotide sequences of Inventions I-VI can be used in a DNA hybridization-binding assay instead of making the polypeptide sequences in Inventions X-XV or the transgenic animals in inventions XVI-XXII. Furthermore, the nucleotide sequences of inventions I-VI can be used in materially different processes as listed above in the Groups VII-XXX.

The nucleotide sequences of Inventions I-VI are unrelated because the nucleotide sequences do not appear to share a common structure. Therefore, it would be an undue burden on the examiner to search all the nucleotide sequence, since each gene encodes a distinct functional polypeptide from different species and the USPTO resources are stretched to the limit. Thus, only one patentably distinct nucleotide sequence thereof can be searched per application.

The amino acid sequences of Inventions X-XV unrelated because the amino acid sequences do not appear to share a common structure. Therefore, it would be an undue burden on the examiner to search all the amino acid sequences, since each amino acid sequences encodes a distinct functional polypeptide from different species and the USPTO resources are stretched to the limit. Thus, only one patentably distinct amino acid sequence thereof can be searched per application.

Although there are no provisions under the section for "Relationship of Inventions" in MPEP 806.05 for inventive groups that are directed to different methods, restriction is deemed to

be proper because each of the methods of inventions VII-IX, XXII-XXVIII, and XXX are patentably distinct inventions for the following reasons: Each of the inventions is directed to different goals and comprises materially distinct steps, wherein each of the compositions in each invention is structurally distinct and/or generates distinct mechanisms and functional effects as indicated above. The scope of each of the cited inventions encompasses an employed method, which generates distinct function(s) and effect(s), and furthermore does not necessarily overlap with that of another invention. Invention VII is a method of diagnosing a polymorphism comprising hybridizing a probe of claim 3 to a patient's sample of DNA or RNA. . Invention VIII is a method for diagnosing long QT syndrome using an antibody. Invention IX is a method of diagnosing the presence of a polymorphism in human KCNE2, wherein method is performed by means which identify the presence of said polymorphism. Invention XXIII is an in vitro method to screen for drugs, which are useful in treating a person with a mutation in KCNE2. Invention XXIV is a method to screen drugs, which are useful in treating or preventing long QT syndrome. Invention XXV is a method for diagnosing a polymorphism comprising determining the KCNE2 sequence in a patient. Invention XXVI is a method of assessing a risk in a human subject for long QT comprises screening said subject for a mutation in a KCNE2 gene. Invention XXVII is a method of determining the ability of a drug to affect fast delayed rectifier potassium current. Invention XXVIII is a method for determining the correlation between inheritance of a mutation of KCNE2. Invention XXX is a method of identifying a polymorphic form correlated with long QT syndrome. Each of the inventions VII-IX, XXII-XXVIII, and XXX comprises materially distinct steps, and/or generates different functions and effects, and thus, is not required for use with one another.

Therefore, inventions I-XXX are distinct.

If applicants elect invention XXVII or XXVIII, the applicant is further required to elect a species. Claims 55, 57, and 59 are generic to a plurality of disclosed patentably distinct species comprising mutant KCNE2 gene consisting of a) Gln9>Glu (C25G); b) Met 54>Thr (T161C); c) Ile 57>Thr (T170C); and d) Thr8>Ala (A22G) in claims 56, 58, or 60. Applicant is required under 35 U.S.C. 121 to elect a single disclosed species (a, b, c, or d), even though this requirement is traversed.

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Because these inventions are distinct for the reason given above and have acquired a separate status in the art because of their divergent subject matter, fall into different statutory classes of inventions, and are separately classified and searched, restriction for examination purposes as indicated is proper.

It would be unduly burdensome for the examiner to search and consider patentability of all of the presently pending claims, a restriction for examination purposes as indicated is proper.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 C.F.R. § 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently filed petition under 37 C.F.R. § 1.48(b) and by the fee required under 37 § 1.17(h).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ms. Tracey Johnson whose telephone number is (703) 305-2982.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (703) 305-0775. The examiner can normally be reached on M-F, (730-400 EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Clark can be reached at (703) 305-4051.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 308-8724.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-8724.

Brian Whiteman
Patent Examiner, Group 1633
June 20, 2001

DAVE T. NGUYEN
PRIMARY EXAMINER